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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,773	03/18/2004	Hiroshi Sano	026350-091	8736

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,773	SANO ET AL.	
	Examiner	Art Unit	
	Kagnew H. Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *16* is/are allowed.

6)☐ Claim(s) *17-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/971,020.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

Acknowledgment for priority is made for this application which is a divisional of parent application No. 09/971,020 filed October 5, 2001 now US 6,734,342 which claims priority under 35 U.S.C. § 119 and/or 365 to Japanese Application No. 2000-307149 filed October 6, 2000.

Information Disclosure Statement

The information disclosure statement filed on March 18, 2004 for which copies of the patent, publications were submitted in this application has been received and will be reviewed in full.

Oath/Declaration

The Oath or declaration submitted on March 18, 2004 was reviewed and is acknowledged to be in compliance with 37 CFR 1.63.

Status of Claims

Applicant's request on May 16, 2006 for the status of the application is received. Original claims 1-15 have been cancelled and new claims 16-18 are added. Claims 16-18 are present for examination.

Specification

The amendment to the abstract has not been entered because applicants have not provided marked up copy of the abstract.

On page 6, line 19, the genus and species name must be written with italics as follows: "*Arabidopsis thaliana* L. Heynh".

Throughout the specification (for example page 8 line 12, line 15, 17, 19 etc.) applicants use the recitation "a sequence listing". Such a reference of sequences referring to a specific list in the application should be referred to as "the sequence listing".

On page 9 line 25, the recitation "In concrete, the reaction mixture of 100μl". In the context used, such wording is improper English, wording such as "Specifically, a reaction mixture of 100μl" or "A reaction mixture of 100μl" is suggested.

Page 10 line 31, 7-methylxathine is misspelled.

On page 4, line 27 "...homology 90%..." should read as "...homology of 90%..."

Fig.1 is objected for not being labeled as "Prior Art".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 17 and 18 are under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 and 18 recites the limitation "wherein said polypeptide has been modified by deletion, insertion, or substitution of one or more amino acids". There is

insufficient antecedent basis for this limitation in the claim 16 given that the polypeptide is a full-length polypeptide.

Claim 18 is rejected because of the recitation "homology". The specification does not clarify this term in any specific way. For examination purposes homology between amino acid residues will be understood as identity between amino acid residues. Thus a level of 90% homology will be understood as 90% identical using any comparison program.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polypeptide sequences wherein any number of modifications comprising a deletion, insertion or substitution of one or more amino acids from the polypeptide of SEQ ID NO: 1 or any polypeptide having at least 90% homology to SEQ ID NO: 1. The specification teaches the structure of only a single representative species of such a polypeptide, represented by SEQ ID NO: 1. Moreover, the specification fails to describe any

other representative species by any identifying characteristic or property other than the functionality of having an N-methyltransferase activity using 7-methylxanthine as a substrate.

Furthermore, applicants specification on page 5 line 14 to line 19 teaches that SEQ ID NOs: 3, 5, and 7, which share more than 80% homology with SEQ ID NO: 1, do not exhibit theobromine synthase activity. The specification does not describe the changes that can be made to SEQ ID NOs: 1 while retaining the enzymatic activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 1, does not reasonably provide enablement for any polypeptide having a deletions, insertion or substitutions of one or more amino acids relative to SEQ ID NO: 1, or a polypeptide showing 90% identity to the polypeptide of SEQ ID NO: 1 having an N-methyltransferase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 17 and 18 are so broad as to encompass any polypeptide having a deletions, insertion or substitutions of one or more amino acids relative to SEQ ID NO: 1 or a polypeptide having at least 90% identity to the specific DNA of SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptide sequences broadly encompassed by the claims. Since the amino

acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in the polypeptide sequence and obtain the desired activity of the protein requires a knowledge of and guidance with regard to which amino acid in the polypeptide sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the amino acid structure relates to it's function. However, in this case the disclosure is limited to the polypeptide sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within the polypeptide modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility of the polypeptide (i.e. theobromine synthase activity) are limited in enzymatic protein and the result obtained from such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions or insertion.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of a polypeptide with having one or more amino acid deletions, insertions or substitution or any polypeptide having 90% identity to the theobromine synthase polypeptide of SEQ ID NOS: 1 because the specification does **not** establish: (A) regions of the polypeptide structure which may be modified without effecting activity of the encoded protein; (B) the general tolerance of the polypeptide of SEQ ID NO: 1 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in SEQ ID

NO: 1 with an expectation of obtaining a desired function such as theobromine synthase activity and (D) the lack of guidance in the specification as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a polypeptide with theobromine synthase activity with an enormous number of amino acid modifications (up to 10%) of the reductase of SEQ ID NOS: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a polypeptide having theobromine synthase activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Mizuno et al. US PAT 6,930,227. Claim 17 is broadly drawn to an isolated polypeptide where the polypeptide has been modified by deletion, insertion substitution of one or more amino acids which are able to can synthesize theobromine using 7-methylxanthine as the substrate. Mizuno et al teach an enzyme

having a theobromine synthase activity when 7-methylxanthine was used as a substrate. In addition Muzuno et al's enzyme can also converts theobromine to caffeine. Muzuno's enzyme has 356 amino acid residues and shows 36% identity to the polypeptide of SEQ ID NO: 1 of the instant application thus anticipating claim 17 which claims one or more deletions, insertion or substitution and has theobromine synthase activity.

Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Misako et al . Misako et al. (in IDS) teach purification and characterization of caffeine synthase from tea leaves. Claim 17 is broadly drawn to an isolated polypeptide where the polypeptide has been modified by deletion, insertion or substitution of one or more amino acids which are able to can synthesize theobromine using 7-methylxanthine as the substrate. Misak et al's study discloses a purified enzyme from young tea leaves, which possesses various methyltransferase activities wherein the highest activity was conversion of 7-methylxanthine to theobromine. Although Misako et al did not sequence the amino acid of the entire enzyme, given that this enzyme possess the activity limitation of converting 7-methylxanthine to theobromine and that claim 17 is drawn to an modified polypeptide wherein one or more amino acids are deleted, inserted or substituted and can synthesize theobromine from 7-methylxanthine as the substrate Misako et al's disclosure which has the functional limitation anticipates claim 17.

Conclusion: Claim 16 is allowable.

Relevant références:

US 6734342 B2 Sano et al.. Theobromine synthetase polypeptide of Coffee Plant and the gene encoding said polypeptide.

US 6392125 B1 Sano et al. Method for producing the transformant of coffee plants and transgenic coffee plants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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